Book Reviews

Synthetic Aspects of Biologically Active Cyclic Peptides. By N. Izumiya, T. Kato, H. Aoyagi, M. Waki, and M. Kondo. Halsted Press (Wiley), New York. 1979. xii + 166 pp. 22.5 × 15 cm. $29.95.

Low-molecular-weight peptides produced by microorganisms have long interested peptide chemists since these compounds often possess interesting structures and useful biological activities. This field has expanded recently as modern separation and analytical methods have facilitated the characterization of labile peptides found in small quantities in nature.

This book addresses the chemistry of cyclic peptides produced by microorganisms. In Chapter 1, microbial peptides are briefly classified by structure. The isolation and structure determination of gramicidin S and the related peptides, tyrocidines, linear gramicidins, gramicidin J, and gratisin, are summarized in Chapter 2. The chemical synthesis and structure–activity relationships of these peptides are described in detail in Chapters 3 and 4. Chapter 5 covers recent studies on the conformation of the peptide antibiotics by many methods, including X-ray, ORD, CD, NMR, and IR, while Chapters 6 and 7 describe mechanism of action and biosynthesis studies of gramicidin S and tyrocidines. These chapters are covered in a clear and accurate but brief fashion. Chapter 8 presents a very nice discussion of the recent synthesis of the phytotoxins AM-toxin I, II, and III and of Cyl-2 toxin, which together are reviewed for the first time.

As noted in the introduction, the authors have made substantial contributions to the synthetic chemistry of these cyclic peptides and this book emphasizes the chemistry developed in their laboratories. Many interesting and useful synthetic methods have been discovered in the course of their studies of the gramicidins and tyrocidines, and these clearly will be useful for synthesizing other cyclic peptide systems. This is a well-written book by a leading group of peptide chemists, who manage to generate substantial interest in cyclic peptides by their multifaceted approach to the subject. I would expect this book to be of interest both to beginning and experienced peptide chemists.

The University of Wisconsin—Madison **Daniel H. Rich**

Neuronal Information Transfer. Edited by A. Karlen, V. M. Tennyson, and H. J. Vogel. Academic Press, New York. 1978. xx + 459 pp. 16 x 23 cm. $42.50.

The chemical basis of nerve transmission has been the most intensely investigated aspect of neurochemistry for nearly 3 decades. A vast increase in our understanding of the nature of neurotransmission, including the variety of neurotransmitters, the regulation of their synthesis, storage, release and degradation, and their receptors has occurred. The complexity so far unfolded is staggering; yet it is clear to most students of this dynamic field that we have just begun the process of understanding the divine mystery of "neuronal information transfer".

The volume at hand, stemming from papers presented at a June, 1977, meeting at Columbia University, might appear dated in such a fast-moving field. Obviously, only rapid communication journals can provide the "latest" information in so rapidly moving an area of research for those who cannot or chose not to attend meetings. This volume will prove of value to many interested in getting a broad view of neurotransmitter and receptor mechanisms, as well as to many investigators as a source of earlier references.

The book is organized into six sections: (1) biogenic amines, (2) cholinergic systems, (3) amino acid systems, (4) brain peptides and opiate systems, (5) cyclic nucleotides, and (6) neuronal structure and development. The 25 papers in these 6 sections are authored by many of the outstanding investigators in this field: Axelrod, Glowinski, Lefkowitz, Nachmanson, Rees, Roberts, Simon, and Snyder.

The majority of the articles are relatively brief review articles rather than presentations of new data that might more appropriately appear in journals. They provide an excellent basis for understanding how we arrived at the current generation of studies of neuronal information transfer.

University of Chicago **Herbert Y. Meltzer**

NMR and Biochemistry. A Symposium Honoring Mildred Cohn. Edited by S. J. Opella and P. Lu. Marcel Dekker, New York and Basel. 1979. xii + 434 pp. 16 × 23.5 cm. $45.00.

Over the past decade, NMR has become an important research tool for biochemists. During the previous decade, Mildred Cohn pioneered the use of NMR in the study of enzyme mechanisms. This symposium, held in her honor (June 22–23, 1978), illustrates the subsequent extension of biochemical applications of NMR for investigating the details of enzyme actions and beyond to more diverse experimental problems. These proceedings of that symposium contain 28 review-type papers (average length, 15 pages) which are predominantly overviews and updates of the contributors' investigations. The volume is organized into four general topic areas, viz., proteins and nucleic acids, strategies for biological NMR, membranes and intact cells, and enzymes.

Highlights of the volume begin with Dr. Cohn's historical development of her work with enzyme reactions involving phosphate compounds and, more recently, the use of ^{18}O-induced isotopic shifts in the ^{31}P NMR spectrum of phosphates to follow enzyme-catalyzed [^{18}O]phosphate–water exchange. Allerhand and co-workers illustrate the application of natural abundance ^{13}C NMR toward understanding the short-range properties of proteins in solution. Schimmael's studies on the topography of protein binding to transfer RNA are followed by Reid and co-workers' investigations of tRNA conformation and base-pair sequencing. Jardetzky presents the experimental and theoretical considerations for NMR relaxation studies of the internal motion of proteins. The advantages and disadvantages of going to higher magnetic fields are delineated by Bothner-By and Dadok. Waugh discusses the methods to circumvent line broadening in the NMR of solid samples. These latter three papers are of general and lasting interest. McConnell's brief description of his studies on lateral molecular motion in lipid bilayers includes his more recent photobleaching–relaxation approaches. Chance and co-workers review their recent ^{31}P NMR investigation of brain tissues, which unfortunately is the only paper on NMR of intact cells or organs. The enzymes section emphasizes active-site conformation of substrates and active-site mapping using paramagnetic metal ion chelation by phosphate-containing substrates. Mildvan's review of the role of metals in the various mechanisms of ATP utilizing enzymes highlights this section.

In addition to serving as a reference source for specific topics, this symposium volume is an excellent introduction for NMR spectroscopists to the biochemical applications of NMR and for biochemists to the utility of NMR spectroscopy. It is of particular value to students and teachers pursuing enzyme mechanisms.

Case Western Reserve University **Dorr G. Dearborn**

Annual Review of Neurochemistry. Volume 3. Edited by W. M. Cowan, Z. H. Hall, and E. R. Kandell. Annual Reviews Inc., Palto Alto, CA. 1980. 428 pp. 15.5 × 23 cm. $17.00.

This volume is the third of a series of "Annual Reviews" devoted to the rapidly burgeoning and expanding area of neurosciences. A number of the chapters are neuroanatomical and neurophysiological in nature dealing with such specialized, but timely, topics as developmental neurobiology in invertebrates, visual-motor function in primates, trophic factors in neurogenesis, and the

factors involved in cellular and neuromuscular specificity. Such chapters make little reference to the biochemical or pharmacological aspects of the problems. A chapter entitled "Soma Currents" is devoted to the methodological and kinetics aspects of the specific ionic currents associated with the nerve action potential. The chapter on chemical neurotoxins is a critical, comprehensive one dealing with the chemistry and mechanisms of action of neurotoxins used to specifically affect neurotransmitter systems such as catecholamines, serotonin, and glutamic acid. The chapter on substance P reviews the neuroanatomical and neurophysiological evidence in support of the neuropeptide's role as an excitatory neurotransmitter in sensory and other afferent neural pathways. An interesting, provocative chapter by D. Koshland is devoted to a discussion of the biochemical mechanisms of chemotaxis in bacteria and implications for understanding neuronal communication in higher organisms. The last chapter presents a scholarly, critical review of the biochemistry and mechanism of action of the nerve growth factor, a high-molecular-weight protein chemically related to proinsulin and presumed to play a role in the development of certain nerve cells. With the possible exception of the chapters on bacterial chemotaxis, neurotoxins, and nerve growth factor, the remainder may be of limited value to the medicinal chemist, except for those with specialized interests. Most of the chapters are well-written and provide selective, updated references.

University of Rochester **L. G. Abood**

Advances in Pharmacology and Chemotherapy. Volume 16. Edited by S. Garattini, A. Goldin, F. Hawking, and I. J. Kopin. Academic Press, New York. 1979. x + 302 pp. 16 x 23.5 cm. $31.00.

This volume is a collection of seven reviews written by 14 contributors. Each of these reviews appears to provide a valuable status report on recent advances in highly specialized areas of pharmacological interest. However, it is very unlikely that any investigator would be interested in any more than one of the reviews contained because the topics are diverse and not obviously related. For instance, an elegant review of the mechanism of action of the benzodiazepines is preceded by new experimental antimalarials and followed by resistance to anthelmintics. Although few are likely to purchase this volume for a personal library, this volume, as well as the rest of the series, has an important place in a biomedical or pharmaceutical library.

Northeastern University **Norman R. Boisse**

Computer-Assisted Drug Design. ACS Symposium Series. Number 12. Edited by Edward C. Olson and Ralph E. Christoffersen. American Chemical Society, Washington, D.C. 1979. xii + 619 pp. 15 × 23 cm. $40.00.

This book is based on a symposium sponsored by the Divisions of Computers in Chemistry and Medicinal Chemistry at the ACS/CSJ Chemical Congress, Honolulu, Hawaii, April 2-6, 1979. It includes 26 chapters by 66 authors; ten of the papers for which abstracts were listed in the program are not included in the volume.

This book is typical of symposium volumes in that the depth of detail and the degree of inclusion of previously or subsequently pulished information in the chapters is variable and that, although most chapters represent state of the art work, the field is not covered in a systematic way. In spite of these not unexpected limitations, it serves a useful purpose both for those already using computers in their drug-design program and for those who wonder if they should be doing so. The first two chapters are reviews: the first a short one of quantum pharmacology in the period 1976-1978 by Christoffersen, and the second a general review of parameters and methods in quantitative structure-activity relationships (linear free energy analysis) by Osman, Weinstein, and Green. The other chapters illustrate the many types of uses made of computers in drug design and give one a sense of the possibilities for other applications. The type of applications discussed is wide: quantum chemical applications are represented by inclusion in nine papers; the utility of electrostatic potential maps generated from quantum chemical calculations by four; the calculation of conformation by potential energy or molecular mechanics methodology by eight; the possible methodology of the quantitative assessment of the similarity or difference in conformation of two molecules by seven; examples of computer graphics for the display of three-dimensional structure of drugs, transition states in enzymatic reactions, or protein receptors by eight; the use of statistical or pattern-recognition methods for the quantitation of relationships between chemical or conformational properties and drug potency by seven; and the computer-assisted design of synthetic pathways by four. Aside from the reviews, the following types of molecules are considered: steroids, opiates, carcinogens, inhibitors of chorismate mutase, LSD, substrates of alcohol dehydrogenase, substrates and inhibitors of serine proteases, centrally acting dopaminergic compounds, compounds that stimulte insulin release from pancreatic islets, cardenolides, thyroid hormones, acetylcholine, clofibrate analogues, conformationally defined analogues of methamphetamine, pyridine carbaldoximes, antitumor compounds, phenols, and uncouplers of oxidative phosphorylation.

Of interest to industrial medicinal chemists will be the chapters which describe the uses of computers in drug design at Upjohn (Duchamp), Rohm and Haas (Stuper, Dyott and Zander), and ROUSSEL-UCLAF (Cohen) and a review of the Merck experience with computer-assisted design of synthetic pathways (Gund, Grabowski, Smith, Andose, Rhodes, Wipke).

The major deficiency in the book is the index: authors are not included, and subjects are indexed incompletely and inconsistently.

Abbott Laboratories **Yvonne C. Martin**

Stereodynamics of Molecular Systems. Edited by R. H. Sarma. Pergamon Press, New York, Oxford, Toronto, Sydney, Frankfurt, and Paris. 1979. xi + 460 pp. 25 × 17 cm. $50.00.

This volume contains 27 papers presented at a conference held at the State University of New York at Albany, April 23-24, 1979. Stereodynamics, in case one is not quite sure, refer to studies concerned with structural and/or dynamical properties of molecules. This, of course, makes for a rather inclusive topic, and the attempt is here made to be comprehensive in its treatment. Thus, individual contributions range from the study of ions and small molecules to macromolecules and even to intact organisms.

The book is divided into five parts. The first section is devoted to methodology and includes three articles on nuclear magnetic resonance and one on X-ray crystallography. The next four sections take up molecular systems in order of increasing complexity. Thus, small molecules and ions are treated in Part II, followed by medium-sized systems, such as cyclic tripeptides, organotransitions metal complexes, and crown complexes, in Part III. These two sections draw heavily upon nuclear magnetic resonance. Part IV progresses to biomolecules, and here the emphasis shifts to an in-depth examination of one particular type molecular system—nucleic acids. This section is the heart of this volume. Thirteen of the 27 papers are on nucleic acid stereodynamics. The "centerpiece" of this section is a series of color plates which beautifully depict nucleic acid structures. These include stereoillustrations of various DNA forms and an illustration of the structure of yeast phenylalanine transfer RNA. Much of the discussion throughout this section benefits from these illustrations. The final section obligatorily progresses to "Intact Biological Systems". Only two contributions are, however, found in this section: one on NMR of solids using magic angle spinning and cross polarization techniques and the other on NMR imaging. The treatment here is cursory and the orientation is primarily on the methodology and is geared to the reader who is unfamiliar with the potential of these techniques.

The net result of such an ambitious undertaking is that this volume lacks a real focus. Nevertheless, many of the individual contributions are very good and should be of interest to a wide range of readers. The overall emphasis, however, is on nucleic acid "stereodynamics", and those interested in a detailed and up-to-date treatise on this subject should find this volume valuable.

Tufts University School of Medicine **William W. Bachovchin**